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 NEWS  1           Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2           "Ask CAS" for self-help around the clock
 NEWS  3  DEC 21   IPC search and display fields enhanced in CA/CAplus with the
                   IPC reform
 NEWS  4  DEC 23   New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/
                   USPAT2
 NEWS  5  JAN 13   IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
 NEWS  6  JAN 13   New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to
                   INPADOC
 NEWS  7  JAN 17   Pre-1988 INPI data added to MARPAT
 NEWS  8  JAN 17   IPC 8 in the WPI family of databases including WPIFV
 NEWS  9  JAN 30   Saved answer limit increased
 NEWS 10  JAN 31   Monthly current-awareness alert (SDI) frequency
                   added to TULSA
 NEWS 11  FEB 21   STN AnaVist, Version 1.1, lets you share your STN AnaVist
                   visualization results
 NEWS 12  FEB 22   Status of current WO (PCT) information on STN
 NEWS 13  FEB 22   The IPC thesaurus added to additional patent databases on STN
 NEWS 14  FEB 22   Updates in EPFULL; IPC 8 enhancements added
 NEWS 15  FEB 27   New STN AnaVist pricing effective March 1, 2006
 NEWS 16  FEB 28   MEDLINE/LMEDLINE reload improves functionality
 NEWS 17  FEB 28   TOXCENTER reloaded with enhancements
 NEWS 18  FEB 28   REGISTRY/ZREGISTRY enhanced with more experimental spectral
                   property data
 NEWS 19  MAR 01   INSPEC reloaded and enhanced
 NEWS 20  MAR 03   Updates in PATDPA; addition of IPC 8 data without attributes
 NEWS 21  MAR 08   X.25 communication option no longer available after June 2006
 NEWS 22  MAR 22   EMBASE is now updated on a daily basis

 NEWS EXPRESS  FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,
               CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.
               V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT
               http://download.cas.org/express/v8.0-Discover/

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FILE 'HOME' ENTERED AT 06:50:56 ON 24 MAR 2006

=> file reg
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	1.47	1.47

FILE 'REGISTRY' ENTERED AT 06:55:10 ON 24 MAR 2006

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 22 MAR 2006 HIGHEST RN 877759-05-2
DICTIONARY FILE UPDATES: 22 MAR 2006 HIGHEST RN 877759-05-2

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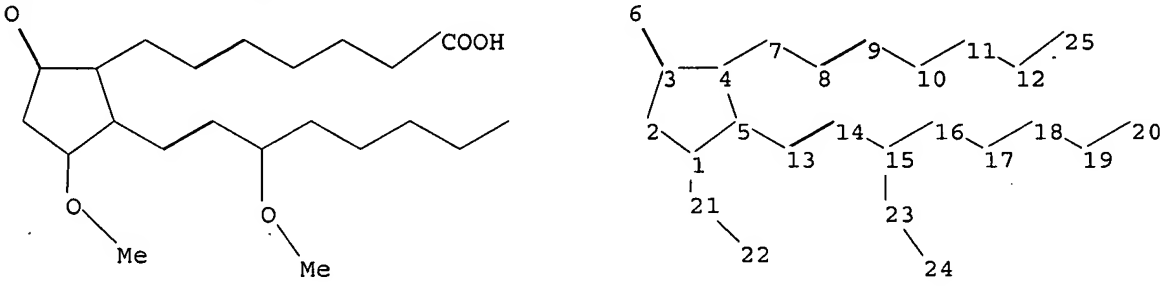
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
****

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=>
Uploading C:\Documents and Settings\mgraffeo\My Documents\Critical Data\10530752\cmp1.str



chain nodes :
6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25
ring nodes :
1 2 3 4 5
chain bonds :
1-21 3-6 4-7 5-13 7-8 8-9 9-10 10-11 11-12 12-25 13-14 14-15 15-16
15-23 16-17 17-18 18-19 19-20 21-22 23-24

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ring bonds :
1-2  1-5  2-3  3-4  4-5
exact/norm bonds :
1-2  1-5  1-21  2-3  3-4  3-6  4-5  15-23
exact bonds :
4-7  5-13  7-8  8-9  9-10  10-11  11-12  12-25  13-14  14-15  15-16  16-17  17-18
18-19  19-20  21-22  23-24


Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:CLASS  7:CLASS  8:CLASS  9:CLASS
10:CLASS  11:CLASS  12:CLASS  13:CLASS  14:CLASS  15:CLASS  16:CLASS  17:CLASS
18:CLASS  19:CLASS  20:CLASS  21:CLASS  22:CLASS  23:CLASS  24:CLASS  25:CLASS



L1      STRUCTURE UPLOADED

=> s l1
SAMPLE SEARCH INITIATED 06:56:13 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -       48 TO ITERATE

100.0% PROCESSED       48 ITERATIONS                                1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          545 TO     1375
PROJECTED ANSWERS:               1 TO       80

L2            1 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 06:56:16 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -     1118 TO ITERATE

100.0% PROCESSED     1118 ITERATIONS                                4 ANSWERS
SEARCH TIME: 00.00.01

L3            4 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                               167.38     168.85

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FILE LAST UPDATED: 22 Mar 2006  (20060322/ED)
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=> s l3
L4          27 L3

=> s l4 (L) (prostaglandin or EP3)
         68216 PROSTAGLANDIN
           984 EP3
L5          19 L4 (L) (PROSTAGLANDIN OR EP3)

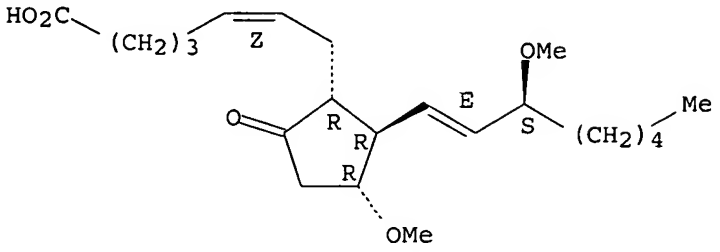
=> s l5 and allergy
         42523 ALLERGY
L6           1 L5 AND ALLERGY

=> d bib abs hitstr

L6   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2006 ACS on STN
AN   2004:333600  CAPLUS
DN   140:344925
TI   Remedies for allergic diseases containing EP3 receptor agonists
IN   Narumiya, Shuh
PA   Ono Pharmaceutical Co., Ltd., Japan
SO   PCT Int. Appl., 60 pp.
     CODEN: PIXXD2
DT   Patent
LA   Japanese
FAN.CNT 1
     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
PI   WO 2004032964         A1    20040422    WO 2003-JP12980         20031009
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
             GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
             TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     AU 2003272962         A1    20040504    AU 2003-272962          20031009
     EP 1563845            A1    20050817    EP 2003-754059          20031009
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
PRAI JP 2002-297900        A     20021010
     WO 2003-JP12980       W     20031009
OS   MARPAT 140:344925
AB   Disclosed is a preventive and/or a remedy for allergic diseases containing a
     compound having an agonistic activity to EP3 receptor which is one of
     prostaglandin E2 receptor subtypes.  More specifically speaking, a compound
     having an agonistic activity to EP3 receptor is efficacious in treating
     allergic respiratory diseases such as bronchial asthma, infantile asthma,
     allergic asthma and atopic asthma.  Moreover, it is expected that a highly
     selective compound would exert a more remarkable therapeutic effect.  The
     effect of 11α,15α-dimethoxy-9-oxoprosta-5Z,13E-dienoic acid
     (I) in OVA-induced asthma model mice was examined  Also, a tablet containing I
     0.5 mg/tablet was prepared
IT   211230-67-0
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (remedies for allergic diseases containing EP3 receptor agonists)
```

RN 211230-67-0 CAPLUS
CN Prosta-5,13-dien-1-oic acid, 11,15-dimethoxy-9-oxo-,
(5Z,11α,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s l5 and allerg?
65253 ALLERG?
L7 1 L5 AND ALLERG?

=> s l5 and (asthma or "hay fever" or reaction or hypersensitivity)
30341 ASTHMA
14664 "HAY"
27656 "FEVER"
1408 "HAY FEVER"
("HAY"(W)"FEVER")
2893439 REACTION
20307 HYPERSENSITIVITY
L8 2 L5 AND (ASTHMA OR "HAY FEVER" OR REACTION OR HYPERSENSITIVITY)

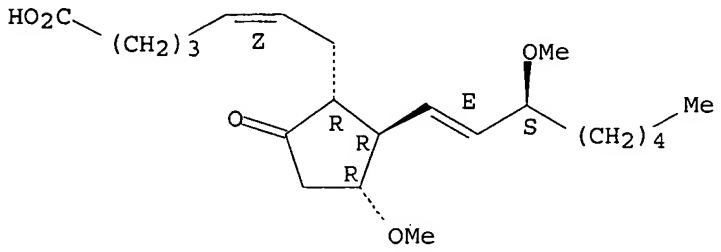
=> d 1-2 bib abs hitstr

L8 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:333600 CAPLUS
DN 140:344925
TI Remedies for allergic diseases containing EP3 receptor agonists
IN Narumiya, Shuh
PA Ono Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004032964	A1	20040422	WO 2003-JP12980	20031009
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003272962	A1	20040504	AU 2003-272962	20031009
EP 1563845	A1	20050817	EP 2003-754059	20031009
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
PRAI JP 2002-297900 A 20021010
WO 2003-JP12980 W 20031009
OS MARPAT 140:344925
AB Disclosed is a preventive and/or a remedy for allergic diseases containing a compound having an agonistic activity to EP3 receptor which is one of prostaglandin E2 receptor subtypes. More specifically speaking, a compound having an agonistic activity to EP3 receptor is efficacious in treating allergic respiratory diseases such as bronchial **asthma**, infantile **asthma**, allergic **asthma** and atopic **asthma**. Moreover, it is expected that a highly selective compound would exert a more remarkable therapeutic effect. The effect of 11α,15α-dimethoxy-9-oxoprosta-5Z,13E-dienoic acid (I) in OVA-induced **asthma** model mice was examined Also, a tablet containing I 0.5 mg/tablet was prepared
IT **211230-67-0**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(remedies for allergic diseases containing **EP3** receptor agonists)
RN 211230-67-0 CAPLUS
CN Prosta-5,13-dien-1-oic acid, 11,15-dimethoxy-9-oxo-, (5Z,11α,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

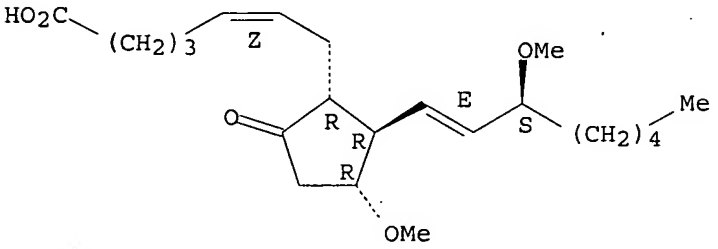
L8 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:101602 CAPLUS
DN 138:332109
TI Mechanisms of cytosolic Ca2+ suppression by prostaglandin E2 receptors in rat melanotrophs
AU Nagata, T.; Harayama, N.; Sasaki, N.; Inoue, M.; Tanaka, K.; Toyohira, Y.; Uezono, Y.; Maruyama, T.; Yanagihara, N.; Ueta, Y.; Shibuya, I.
CS Department of Physiology, School of Medicine, University of Occupational and Environmental Health, Kitakyushu, 807-8555, Japan
SO Journal of Neuroendocrinology (2003), 15(1), 33-41
CODEN: JOUNE2; ISSN: 0953-8194
PB Blackwell Science Ltd.
DT Journal
LA English
AB The authors have previously reported that voltage-dependent Ca2+ (VDC) channels of rat melanotrophs are inhibited by prostaglandin E2 (PGE2). In this study, mechanisms involved in the inhibitory actions of PGE2 receptors of rat melanotrophs were analyzed using reverse transcriptase-polymerase chain **reaction** (RT-PCR), Ca2+-imaging and whole-cell, patch-clamp techniques with recently developed EP agonists, each of which is selective for the known four subclasses of EP receptors (EP1-4). PGE2 reversibly suppressed the cytosolic Ca2+ concentration ([Ca2+]i). The maximum reduction in [Ca2+]i by PGE2 was comparable to that by dopamine or to that by extracellular Ca2+ removal. RT-PCR anal. of all four EP receptors revealed that EP3 and EP4 receptor mRNAs were expressed

in the intermediate lobe. The effects of PGE2 to suppress [Ca2+]i were mimicked by the selective EP3 agonist, ONO-AE-248, whereas three other EP agonists, ONO-DI-004 (EP1), ONO-AE1-259 (EP2) and ONO-AE1-329 (EP4), had little or no effect on [Ca2+]i. All four G-protein activated inward rectifying K+ (GIRK) channel mRNAs were identified in intermediate lobe tissues by RT-PCR. Dopamine concentration-dependently activated GIRK currents, whereas PGE2 did not activate GIRK currents, even at the concentration causing maximal inhibition of VDC channels. These results suggest that PGE2 acts on EP3 receptors to suppress Ca2+ entry of rat melanotrophs by selectively inhibiting VDC channels of these cells. The authors have compared the possible cellular and mol. mechanisms of inhibition by dopamine and PGE2.

IT **211230-67-0**, ONO-AE-248
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(mechanisms of cytosolic calcium suppression by **prostaglandin** E2 receptors in rat melanotrophs in relation to inhibition by dopamine and PGE2 and role of potassium channels)

RN 211230-67-0 CAPLUS
CN Prosta-5,13-dien-1-oic acid, 11,15-dimethoxy-9-oxo-, (5Z,11α,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> s l5 and prostaglandin
         68216 PROSTAGLANDIN
L9          15 L5 AND PROSTAGLANDIN

=> s prostaglandin (L) allerg?
         68216 PROSTAGLANDIN
         65253 ALLERG?
L10        592 PROSTAGLANDIN (L) ALLERG?

=> s l10 and ("prostaglandin E3" or EP3)
         68216 "PROSTAGLANDIN"
         10159 "E3"
            63 "PROSTAGLANDIN E3"
                 ("PROSTAGLANDIN"(W)"E3")
           984 EP3
L11         14 L10 AND ("PROSTAGLANDIN E3" OR EP3)

=> d 1-14 bib abs
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L11 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2006:261421 CAPLUS
TI Roles of **prostaglandin** D2 and **prostaglandin** E2 in **allergic** reactions: pro-**allergic** and anti-**allergic** modulating pathways
AU Segi-Nishida, Eri
CS Department of Pharmacology, Faculty of Medicine, Kyoto University, Kyoto, Japan

SO Ensho, Saisei (2006), 26(1), 29-34
CODEN: ENSHCC; ISSN: 1346-8022
PB Nippon Ensho-Saisei Igakkai
DT Journal
LA English
AB **Prostaglandin**(PG) D2 and PGE2 are major cyclooxygenase metabolites of arachidonic acid produced during **allergic** reactions including asthma. However, the role of PGD2 and PGE2in **allergic** inflammation has long been ambiguous. This is partly because non-steroidal anti-inflammatory drugs that inhibit prostanoid synthesis are generally ineffective in **allergic** disorders. Both PGs exert their actions by acting on G-protein-coupled receptors; PGD2 acts at the PGD receptor(DP), PGE2 acts at four subtypes of PGE receptor, EP1 to EP4. To dissect the roles of PGD2-DP pathway and each PGE2-EP pathway in **allergic** reactions, we subject mice deficient in DP, EP1, EP2, **EP3** and EP4 receptor individually to ovalbumin-induced **allergic** asthma as a model of type I **allergy.** These studies have revealed that there are opposing actions between two prostanoid pathways in **allergic** reactions; PGD2-DP pathway and PGE2-**EP3** pathway. We found that the PGD2 is an important mediator of **allergic** responses and that PGE2-**EP3** signaling neg. regulates progression of **allergic** inflammation. This review focuses on the opposite roles of these prostanoid path- ways in **allergic** reactions obtained by our studies and other studies. These findings suggest that selective manipulation of the prostanoid receptors may be beneficial in treatment of **allergic** diseases, such as bronchial asthma, **allergic** rhinitis and conjunctivitis.

L11 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:338557 CAPLUS
DN 142:428630
TI Suppression of **allergic** inflammation by the **prostaglandin** E receptor subtype **EP3**
AU Kunikata, Tomonori; Yamane, Hana; Segi, Eri; Matsuoka, Toshiyuki; Sugimoto, Yukihiko; Tanaka, Satoshi; Tanaka, Hiroyuki; Nagai, Hiroichi; Ichikawa, Atsushi; Narumiya, Shuh
CS Department of Pharmacology and Faculty of Medicine and Graduate School of Pharmaceutical Sciences, Kyoto University, Kyoto, 606-8501, Japan
SO Nature Immunology (2005), 6(5), 524-531
CODEN: NIAMCZ; ISSN: 1529-2908
PB Nature Publishing Group
DT Journal
LA English
AB Prostaglandins, including PGD2 and PGE2, are produced during **allergic** reactions. Although PGD2 is an important mediator of **allergic** responses, aspirin-like drugs that inhibit **prostaglandin** synthesis are generally ineffective in **allergic** disorders, suggesting that another **prostaglandin** -mediated pathway prevents the development of **allergic** reactions. Here we show that such a pathway may be mediated by PGE2 acting at the **prostaglandin** E receptor **EP3.** Mice lacking **EP3** developed **allergic** inflammation that was much more pronounced than that in wild-type mice or mice deficient in other **prostaglandin** E receptor subtypes. Conversely, an **EP3**-selective agonist suppressed the inflammation. This suppression was effective when the agonist was administered 3 h after antigen challenge and was associated with inhibition of **allergy** -related gene expression. Thus, the PGE2-**EP3** pathway is an important neg. modulator of **allergic** reactions.
RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:1044002 CAPLUS
DN 142:217217

TI Expression of **prostaglandin** E2 receptor subtypes on cells in sputum from patients with asthma and controls: Effect of **allergen** inhalational challenge
AU Ying, Sun; O'Connor, Brian J.; Meng, Qiu; Woodman, Natalie; Greenaway, Steven; Wong, Helen; Mallett, Kirsty; Lee, Tak H.; Corrigan, Chris
CS From the Department of Asthma, Allergy and Respiratory Science, King's and St Thomas' School of Medicine, UK
SO Journal of Allergy and Clinical Immunology (2004), 114(6), 1309-1316
CODEN: JACIBY; ISSN: 0091-6749
PB Elsevier Inc.
DT Journal
LA English
AB Background: **Prostaglandin** (PG) E2 binds to 4 G-protein-coupled receptors designated EP1 through EP4. Although PGE2 plays an immunomodulatory role in asthma, there is little information on the expression of PGE2 receptors in this disease. Objective: the authors hypothesized that profiles of E-prostanoid (EP) receptor expression are altered on asthmatic bronchial inflammatory cells in vivo and further altered by **allergen** challenge in vivo and proinflammatory mediators in vitro. Methods: The nos. and phenotypes of EP1-4 immunoreactive induced sputum cells from atopic asthmatics (before and 24 h after **allergen** inhalational challenge) and normal controls (3 after saline challenge) and EP1-4 expression on purified blood eosinophils from both groups (for each) before and after stimulation with LPS and/or IL-5 in vitro were measured by using single and double immunocytochem. Results: Subsets of sputum cells of all phenotypes expressed all 4 EP receptors in both patients with asthma and controls. There were significantly greater nos. of macrophages expressing all 4 EP receptors and increased percentages of macrophages expressing EP2 and EP4 in patients with asthma compared with controls. **Allergen** bronchial challenge of patients with asthma was associated with a selective influx of eosinophils, but the percentages of these and other leukocytes expressing all 4 EP receptors were unchanged. Compared with sputum, only small percentages of peripheral blood eosinophils expressed each receptor, but this was increased by culture with exogenous IL-5 or LPS. Conclusion: E-prostanoid receptor expression is increased on airway macrophages of patients with asthma at baseline and may be altered on eosinophils after **allergen** challenge in vivo in response to inflammatory stimuli.
RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:729843 CAPLUS
DN 141:388150
TI Discovery of orally active prostaglandin D2 receptor antagonists
AU Torisu, Kazuhiko; Kobayashi, Kaoru; Iwahashi, Maki; Nakai, Yoshihiko; Onoda, Takahiro; Nagase, Toshihiko; Sugimoto, Isamu; Okada, Yutaka; Matsumoto, Ryoji; Nanbu, Fumio; Ohuchida, Shuichi; Nakai, Hisao; Toda, Masaaki
CS Minase Research Institute, Ono Pharmaceutical Co., Ltd, Shimamoto, Osaka, Mishima, 618-8585, Japan
SO Bioorganic & Medicinal Chemistry Letters (2004), 14(19), 4891-4895
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier B.V.
DT Journal
LA English
OS CASREACT 141:388150
AB A series of N-(p-alkoxy)benzoyl-2-methylindole-4-acetic acids were synthesized and evaluated for **prostaglandin** D2 (DP) receptor affinity and antagonist activity. Some of them exhibited strong receptor binding and were potent in the cAMP formation assays. These antagonists also suppressed **allergic** inflammatory responses such as the PGD2-induced increase of microvascular permeability. Structure-activity relationship (SAR) data are presented.
RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:390250 CAPLUS
DN 140:406734
TI Preparation of pyridopyrrolizines and pyridoindolizines as prostaglandin receptor, in particular PGD2, antagonists
IN Leblanc, Yves; Dufresne, Claude; Roy, Patrick
PA Merck Frosst Canada & Co., Can.
SO PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004039807	A1	20040513	WO 2003-CA1658	20031028
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2503767	AA	20040513	CA 2003-2503767	20031028
	AU 2003275868	A1	20040525	AU 2003-275868	20031028
	EP 1558614	A1	20050803	EP 2003-809672	20031028
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	BR 2003015681	A	20050906	BR 2003-15681	20031028
	JP 2006506457	T2	20060223	JP 2005-501791	20031028
	US 2005272756	A1	20051208	US 2005-532633	20050425
	NO 2005002591	A	20050729	NO 2005-2591	20050527
PRAI	US 2002-422443P	P	20021030		
	US 2003-482626P	P	20030626		
	WO 2003-CA1658	W	20031028		

OS MARPAT 140:406734
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [wherein G = O(CH2)1-2, S(CH2)1-2, (un)substituted C1-3alkyl; Ar = hetero/aryl optionally substituted with Rg; Q = CO2H, CONH2 and derivs., SO2NH2 and derivs., SO3H, PO3H2 and tetrazolyl; one of A, B, C, or D is N and the others are independently selected from CH and CRg; E = (CH2)a-X-(CH2)b, phenylene, cycloalkylidene, cycloalkylene, etc.; a, b = 0-1, X = a bond, O, S, NH and derivs., etc.; F = (CH2)m and derivs., CH:CH and derivs.; m = 1-3; R1 = H, CN, OH and derivs., (un)substituted alkyl, etc.; R2 = H, alkyl optionally substituted with 1-6 halogens; R1R2 = oxo; or R1R2 = (un)substituted 3- or 4-membered ring, optionally containing 1 heteroatom; R3 = H, (un)substituted alkyl; Rg = halo, CN, CHO, CO2H and derivs., CONH2 and derivs., NH2 and derivs., NO2, alkoxy, OCONH2 and derivs., SO2-alkyl, (un)substituted alk/en/yl, etc.] were prepared as **prostaglandin** receptor, in particular PGD2, antagonists useful for the treatment of **prostaglandin**-mediated diseases such as **allergic** rhinitis, nasal congestion and asthma (no data). Six biol. assays are given (no data). Thus, reaction of II (preparation given) with a mixture of bis(3,4-dichlorophenyl)disulfide, SO2Cl2, 1,2-dichloroethane, followed by hydrolysis gave the pyridoindolizinyl acid

III.
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:333600 CAPLUS
DN 140:344925
TI Remedies for allergic diseases containing **EP3** receptor agonists
IN Narumiya, Shuh
PA Ono Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004032964	A1	20040422	WO 2003-JP12980	20031009
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003272962	A1	20040504	AU 2003-272962	20031009
EP 1563845	A1	20050817	EP 2003-754059	20031009
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRAI JP 2002-297900	A	20021010		
WO 2003-JP12980	W	20031009		

OS MARPAT 140:344925
AB Disclosed is a preventive and/or a remedy for **allergic** diseases containing a compound having an agonistic activity to **EP3** receptor which is one of **prostaglandin** E2 receptor subtypes. More specifically speaking, a compound having an agonistic activity to **EP3** receptor is efficacious in treating **allergic** respiratory diseases such as bronchial asthma, infantile asthma, **allergic** asthma and atopic asthma. Moreover, it is expected that a highly selective compound would exert a more remarkable therapeutic effect. The effect of 11α,15α-dimethoxy-9-oxoprosta-5Z,13E-dienoic acid (I) in OVA-induced asthma model mice was examined Also, a tablet containing I 0.5 mg/tablet was prepared
RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:591147 CAPLUS
DN 139:149524
TI Fluoro substituted cycloalkanoindoles, compositions containing such compounds and methods of treatment using them
IN Berthelette, Carl; Lachance, Nicolas; Li, Lianhai; Sturino, Claudio; Wang, Zhaoyin
PA Merck Frosst Canada & Co., Can.
SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003062200	A2	20030731	WO 2003-CA84	20030122

WO 2003062200 A3 20031204
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2003158246 A1 20030821 US 2003-348403 20030121
CA 2471952 AA 20030731 CA 2003-2471952 20030122
BR 2003007050 A 20041026 BR 2003-7050 20030122
EP 1470107 A2 20041027 EP 2003-700740 20030122
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
US 2005124680 A1 20050609 US 2003-502380 20030122
JP 2005518413 T2 20050623 JP 2003-562082 20030122
NO 2004003536 A 20040824 NO 2004-3536 20040824
PRAI US 2002-351384P P 20020124
WO 2003-CA84 W 20030122
OS MARPAT 139:149524
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Fluoro substituted cycloalkanoindole derivs. I [X1 = (O)n; X2 = (CH2)m; n = 0, 1; m = 1 - 3; R1 = H, C1-3-alkyl, C1-3-haloalkyl, cyclopropyl; R2 = C6H4Cl-4, C6H2Cl3-2,4,6], their enantiomers and pharmaceutically acceptable salts, are antagonists of prostaglandins, and as such are useful for the treatment of prostaglandin mediated diseases. Thus, (-)-cyclopentanoindole II was prepared via cyclocondensation of 4-F-2-IC6H3NH2 with Et 2-(2-oxocyclopentyl)acetate, saponification, regioselective bromination, N-alkylation with 4-ClC6H4CH2Br, resolution with (S)-(-)-1-(1-naphthyl)ethylamine, esterification with diazomethane, sulfonylation with MeSO2Na and ester hydrolysis. The binding activity of I for prostaglandin receptors was determined (no data).

L11 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:154382 CAPLUS
DN 138:187795
TI Preparation of aryl or heterocyclyl-substituted benzoic acid and alkanoic acid derivatives as antagonists of prostaglandin E2 (PEG2) receptors
IN Tani, Kousuke; Asada, Masaki; Kobayashi, Kaoru; Narita, Masami; Ogawa, Mikio
PA Ono Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 1009 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003016254	A1	20030227	WO 2002-JP8120	20020808

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2457468	AA	20030227	CA 2002-2457468	20020808
EP 1431267	A1	20040623	EP 2002-755874	20020808
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002011810	A	20040824	BR 2002-11810	20020808
CN 1551866	A	20041201	CN 2002-817376	20020808
NZ 531153	A	20051028	NZ 2002-531153	20020808
ZA 2004000973	A	20050104	ZA 2004-973	20040205
NO 2004000564	A	20040510	NO 2004-564	20040206
PRAI JP 2001-241867	A	20010809		
WO 2002-JP8120	W	20020808		

OS MARPAT 138:187795

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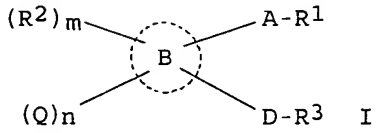

I

AB Carboxylic acid derivs. (I) and nontoxic salts thereof [wherein R1 = CO2H, CO2R4, CH2OH, COR5SO2R6, CONH2, CH2NR5SO2R6, CH2NR9COR10, CH2NR9CONR5SO2R6, CH2SO2NR9COR10, CH2O2CNR5SO2R6, tetrazole, 1,2,4-oxadiazol-5-one, 1,2,4-oxadiazol-5-thione, 1,2,4-thiadiazol-5-one, etc. (wherein R4 = C1-6 alkyl, hydroxy-C1-4 alkyl, C1-4 alkoxy-C1-4 alkyl, carboxy-C1-4 alkyl, etc.; R5, R9 = H, C1-6 alkyl; R6 = C1-6 alkyl, C3-15 mono-, di-, or tricarbocyclic, 3- to 13-membered mono-, di-, or tricyclic heterocyclyl, etc.; R10 = H, R6); A = a single bond, C1-6 alkylene, C2-6 alkenylene, C2-6 alkynylene, etc.; the ring B = C3-12 mono- or dicyclic carbocyclic ring, 3- to 12-membered mono- or dicyclic heterocyclic ring; R2 = C1-6 alkyl, C1-6 alkoxy, C1-6 alkylthio, C2-6 alkenyl, C2-6 alkynyl, halo, CHF2, CF3, NO2, cyano, Ph, oxo; m, n = 0,1,2; Q = (C1-4 alkylene, C2-4 alkenylene, or C2-4 alkynylene)-Cyc2, -C1-4 alkylene-Z-Cyc3, amino-C1-4 alkyl, cyano-C1-4 alkyl, acylamino-C1-4 alkyl, 3- to 7-membered monocyclic carbocyclyl, 3- to 6-membered monocyclic heterocyclyl, etc. (wherein Cyc2, Cyc3 = C3-15 mono-, di-, or tricyclic carbocyclyl or heterocyclyl, etc.; Z = O, S, SO, SO2, NH, NHCO, etc.); D = an linking chain consisting of 1-2 or 3-6 of atoms selected from C, N, O, or S, etc.; R3 = C1-6 alkyl, C3-15 mono-, di-, or tricyclic carbocyclyl, 3- to 15-membered mono-, di-, or tricyclic heterocyclyl, etc.] are prepared These carboxylic acid derivs. include phenylpropanoic acid, phenylpropenoic acid, phenylpropanamide, phenylpropenamide, 3-oxoisoindolin-1-ylacetic acid, benzylbenzoic acid, benzylaminoacetic acid, pyrazolylmethylbenzoic acid, benzoylaminoacetic acid, (pyrazolylmethylphenyl)propenoic acid, pyrazolylmethylpropanoic acid, (pyridinyloxyphenyl)propanoic acid, phenoxyacetic acid, phenylbutanoic acid, (pyrazolylmethyl)propanamide, (piperazinylmethylphenyl)propanamide, (morpholinylmethylphenyl)propanamide , (pyridinyloxyphenyl)propanamide, (pyrazolylmethyl)propenamide (oxoimidazolidinylmethylphenyl)propanamide, (oxopyrrolidinylmethylphenyl)p ropenamide, (thiophenylmethylphenyl)propenamide, (pyrazolylmethylphenylamino)acetamide, (thiazolylaminomethylphenyl)propana mide, thiophenylpropenamide, (pyrazolylmethylphenoxy)acetamide, (phenoxymethyl)benzamide, (pyrazolylmethylphenylethyl)-1,2,4-oxadiazol-5-one, and (pyrazolylmethylphenylindolyl)acetic acid. Because of binding to PEG2 receptors, in particular, subtype **EP3** and/or subtype EP4 and having antagonism, the compds. I are useful in preventing and/or

treating diseases such as pain, allodynia, hyperalgesia, pruritus (itching), urticaria, atopic dermatitis, contact dermatitis, Urushi (Japanese lacquer tree) dermatitis, **allergic** conjunctivitis, symptoms during dialysis, asthma, rhinitis, **allergic** rhinitis, nasal congestion, sneeze, psoriasis, pollakiuria (increased urinary frequency), urination disorder, ejaculation (semination) disorder, fever (pyrexia), systemic inflammation reaction, learning disorder, Alzheimer's disease, neovascularization, cancer formation, cancer proliferation, cancer metastasis to organs, cancer metastasis to bone, hypercalcemia accompanied by cancer metastasis to bone, retinopathy, rubrum, erythema (rash), leucoma, skin moth-patch, heat burn, burn, steroid burn, kidney failure, nephropathy, acute or chronic nephritis, blood electrolyte disorder, imminent abortion, threatened abortion, excessive menstruation, dysmenorrhea, endometriosis, premenstrual syndrome, uterine gland myopathy, reproduction disorder, and stress. They are also useful in preventing and/or treating anxiety, depression, psychophysiol. disorder, mental retardation, thrombus, embolism, transient ischemic attack, cerebral infarction, atheroma, organ transplant, heart failure, hypertension, myocardial infarction, arteriosclerosis, circulation disorders or ulcers associated therewith, nerve disorders, vascular dementia, edema, diarrhea, constipation, biliary excretion disorder, ulcerative colitis, Crohn's disease, irritable bowel syndrome, reduction of rebound after using steroid drugs, aids for decreasing or removing steroid drugs, bone diseases, systemic granuloma, immune diseases, pyorrhea alveolaris, gingivitis, periodontal disease, nerve cell death, lung disorder, liver disorder, acute hepatitis, myocardial ischemia, Kawasaki disease, multiple organ failure, chronic headache, angiitis, venous failure, varicose vein (varicosis), anal fistula, diabetes insipidus, neonatal patent ductus arteriosus, and cholelithiasis. Thus, 4-hydroxymethyl-2-[2-(naphthalen-2-yl)ethoxy]cinnamic acid Et ester was mesylated by methanesulfonyl chloride in the presence of Et3N in THF at 0° for 15 min and condensed with pyrazole in the presence of NaH in DMF at 0° to give 2-[2-(naphthalen-2-yl)ethoxy]-4-(1-pyrazolylmethyl)cinnamic acid Et ester. 4-[2-[[2-(Naphthalen-1-yl)propanoyl]amino]-4-methylthiomethylphenyl]butanoic acid inhibited the binding of [3H]PGE2 to **prostaglandin** E2 (PEG2) receptor subtype EP1, Ep2, **EP3**, and EP4 expressed in CHO cells with Ki of >10, >10, 0.27, and 0.038 μM, resp. A tablet formulation containing (2E)-2-[2-(naphthalen-2-yl)ethoxy]-4-(1-pyrazolylmethyl)cinnamic acid was described.

RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:362587 CAPLUS
DN 136:319468
TI The roles of the prostanoids played in the body
AU Ushikubi, Fumitaka; Narumiya, Shuh
CS Dep. Pharmacol., Asahikawa Med. Coll., Asahikawa, 078-8510, Japan
SO Nippon Yakurigaku Zasshi (2002), 119(4), 201-207
CODEN: NYKZAU; ISSN: 0015-5691
PB Nippon Yakuri Gakkai
DT Journal; General Review
LA Japanese
AB A review. The actions of prostanoids in various physiol. and pathophysiol. conditions have been examined using mice lacking the prostanoid receptors. PGD2 was found to be a mediator of **allergic** asthma. **Prostaglandin** (PG) I2 worked not only as a mediator of inflammation but also as an antithrombotic and cardio-protective agent. Several important actions of PGE2 are brought out via the PGE2-receptor subtype **EP3**; PGE2 participated in the regulation of platelet function, and it worked as a mediator of febrile responses to both endogenous and exogenous pyrogens. These novel findings on the roles of the prostanoids would contribute to the development of drugs targeting the prostanoid receptors.

L11 ANSWER 10 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:185059 CAPLUS
DN 136:232116
TI Preparation of benzoic acid derivatives as prostaglandin E2 receptor antagonists
IN Tani, Kousuke; Asada, Masaki; Kobayashi, Kaoru; Narita, Masami; Ogawa, Mikio
PA Ono Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 114 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002020462	A1	20020314	WO 2001-JP7105	20010820
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 2001078772	A5	20020322	AU 2001-78772	20010820
	CA 2419722	AA	20030221	CA 2001-2419722	20010820
	EP 1314719	A1	20030528	EP 2001-956957	20010820
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2004002493	A1	20040101	US 2003-362878	20030227
PRAI	JP 2000-264889	A	20000901		
	WO 2001-JP7105	W	20010820		

OS MARPAT 136:232116
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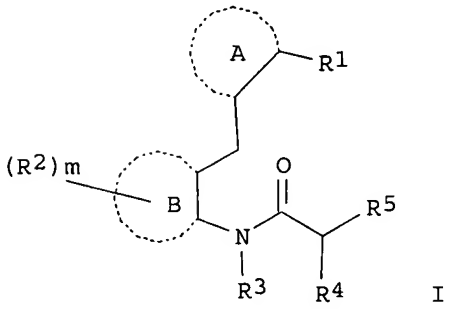

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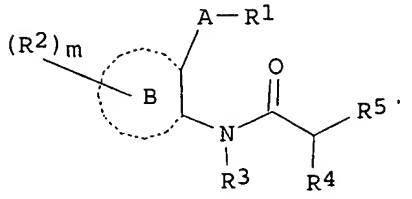
AB The title compds. I [R1 represents COOH, etc.; ring A and ring B each represents a carbon ring or a heterocycle; R2 represents alkyl, alkenyl, alkynyl, etc.; R3 represents H, alkyl; R4 represents alkyl, cycloalkyl, etc.; and R5 represents a carbon ring or a heterocycle; m is 0 - 2] are prepared I are antagonists of PGE2 receptors, in particular, subtypes **EP3** and/or EP4 and are useful in the treatment of pain, allergy, Alzheimer's disease, cancer, etc. In an in vitro test for EP4 receptor antagonism, 2-[2-[2-(4-benzyloxyphenyl)propanoylamino]phenyl]methylbenzoic acid showed the Ki value of 0.01 μM. A formulation is given.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 11 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:157726 CAPLUS
DN 136:216543
TI ° Carboxylic acid derivatives as prostaglandin E2 receptor antagonists and process for preparing them
IN Tani, Kousuke; Asada, Masaki; Kobayashi, Kaoru; Narita, Masami; Ogawa, Mikio
PA Ono Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002016311	A1	20020228	WO 2001-JP7104	20010820
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001078771	A5	20020304	AU 2001-78771	20010820
CA 2420042	AA	20030218	CA 2001-2420042	20010820
EP 1312601	A1	20030521	EP 2001-956956	20010820
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003216381	A1	20031120	US 2003-344989	20030220
US 6835752	B2	20041228		
US 2004235825	A1	20041125	US 2004-864545	20040610
US 2005026908	A1	20050203	US 2004-924924	20040825
PRAI JP 2000-251365	A	20000822		
WO 2001-JP7104	W	20010820		
US 2003-344989	A3	20030220		

OS MARPAT 136:216543
GI



I

AB The title compds. I [R1 represents CO2H, etc.; A represents alkylene, etc.; R2 represents alkyl, alkenyl, alkynyl, etc.; m = 0 - 2; ring B represents a heterocycle, etc. ; R3 represents H, alkyl; R4 represents alkyl, cycloalkyl, etc.; and R5 represents a carbon ring or a heterocycle] are prepared I are antagonists of PGE2 receptors, in particular, subtypes EP3 and/or EP4 and are useful in the treatment of pain, allergy, Alzheimer's disease, cancer, etc. In an in vitro test for EP4 receptor antagonism, 4-[2-[2-(1-naphthyl)propanoylamino]phenyl]butanoic acid showed the Ki value of 0.3 μM. A formulation is given.
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:51982 CAPLUS

DN 136:96105
TI Use of cox-2 inhibitors to treat sepsis, complications thereof, and pros EP receptor modulation
IN Mack Strong, Vivian E.; Stapleton, Philip P.; Daly, John M.
PA USA
SO U.S. Pat. Appl. Publ., 39 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2002006915	A1	20020117	US 2001-782936	20010214
PRAI US 2000-182524P	P	20000215		

AB The present invention is directed to methods of preventing, inhibiting, reversing and/or ameliorating complications in those having or at risk for systemic inflammatory response syndrome, e.g., sepsis, including multiple organ dysfunction syndrome, pancreatitis, burns, trauma, and complications of sepsis such as bacteremia, pneumonia, urinary tract infections, wound infections, and drug reactions. The methods comprise administration of an effective amount of at least one of a selective inhibitor of cyclooxygenase-2, a drug which stimulates one or more PGE2 receptors or a drug which interferes with binding of PGE2 to one of more PGE2 receptors.

L11 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:609702 CAPLUS
DN 133:232942
TI Roles of prostanoids revealed from studies using mice lacking specific prostanoid receptors
AU Ushikubi, Fumitaka; Sugimoto, Yukihiko; Ichikawa, Atsushi; Narumiya, Shuh
CS Department of Pharmacology, Asahikawa Medical College, Asahikawa, 078-8510, Japan
SO Japanese Journal of Pharmacology (2000), 83(4), 279-285
CODEN: JJPAAZ; ISSN: 0021-5198
PB Japanese Pharmacological Society
DT Journal; General Review
LA English
AB A review, with 61 refs. The actions of prostanoids in various physiol. and pathophysiol. conditions have been being examined using mice lacking different prostanoid receptors. **Prostaglandin** (PG) I2 worked not only as a mediator of inflammation but also as an antithrombotic agent. PGF2α was found to be an essential inducer of labor. Several important actions of PGE2 are exerted via each of the four PGE2 receptor subtypes: EP1, EP2, **EP3** and EP4. PGE2 participated in colon carcinogenesis via the EP1. PGE2 also participates in ovulation and fertilization and contributes to the control of blood pressure under high-salt intake via the EP2. PGE2 worked as a mediator of febrile responses to both endogenous and exogenous pyrogens and as a regulator of bicarbonate secretion induced by acid-stimulation in the duodenum via the **EP3**. It regulated the closure of ductus arteriosus and showed bone resorbing action via the EP4. PGD2 was found to be a mediator of **allergic** asthma. These studies have revealed important roles of prostanoids, some of which had not previously been known.
RE.CNT 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1996:607737 CAPLUS
DN 125:293831
TI Prostaglandin E2 receptors of the EP2 and EP4 subtypes regulate activation and differentiation of mouse B lymphocytes to IgE-secreting cells
AU Fedyk, Eric R.; Phipps, Richard P.
CS Department Microbiology Immunology, University Rochester School Medicine Dentistry, Rochester, NY, 14642, USA
SO Proceedings of the National Academy of Sciences of the United States of

America (1996), 93(20), 10978-10983
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
AB **Prostaglandin** E2 (PGE2) is a potent lipid mol. with complex proinflammatory and immunoregulatory properties. PGF2 can shape the immune response by stimulating the production of IgE antibody by B lymphocytes and the synthesis of T-helper type 2 cytokines [e.g., interleukin (IL)-4, IL-10], while inhibiting production of Th1 cytokines (e.g., interferon-γ, IL-12). It is unknown what type of receptor binds PGF2 and modulates these responses. Recent analyses in nonhematopoietic cells have identified six PGE2 receptors (EP1, EP2, **EP3**.alpha., **EP3**.beta., **EP3**.gamma., and EP4). This investigation examines quiescent B lymphocytes and reports that these cells express mRNA encoding EP1, EP2, **EP3**.beta., and EP4 receptors. The immunoregulatory functions of each receptor were investigated using small mol. agonists that preferentially bind EP receptor subtypes. Unlike agonists for EP1 and **EP3**, agonists that bound EP2 or EP2 and EP4 receptors strongly inhibited expression of class II major histocompatibility complex and CD23 and blocked enlargement of mouse B lymphocytes stimulated with IL-4 and/or lipopolysaccharide. PGE2 promotes differentiation and synergistically enhances IL-4 and lipopolysaccharide-driven B-cell Ig class switching to IgE. Agonists that bound EP2 or EP2 and EP4 receptors also strongly stimulated class switching to IgE. Expts. employing inhibitors of cAMP metabolism demonstrate that the mechanism by which EP2 and EP4 receptors regulate B lymphocyte activity requires elevation of cAMP. In conclusion, these data suggest that antagonists to EP2 and EP4 receptors will be important for diminishing **allergic** and IgE-mediated asthmatic responses.

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	87.54	256.39

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-12.75	-12.75

STN INTERNATIONAL LOGOFF AT 07:02:24 ON 24 MAR 2006

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssptamxg1614

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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1           Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2           "Ask CAS" for self-help around the clock
 NEWS  3  DEC 21   IPC search and display fields enhanced in CA/CAplus with the
                   IPC reform
 NEWS  4  DEC 23   New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/
                   USPAT2
 NEWS  5  JAN 13   IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
 NEWS  6  JAN 13   New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to
                   INPADOC
 NEWS  7  JAN 17   Pre-1988 INPI data added to MARPAT
 NEWS  8  JAN 17   IPC 8 in the WPI family of databases including WPIFV
 NEWS  9  JAN 30   Saved answer limit increased
 NEWS 10  JAN 31   Monthly current-awareness alert (SDI) frequency
                   added to TULSA
 NEWS 11  FEB 21   STN AnaVist, Version 1.1, lets you share your STN AnaVist
                   visualization results
 NEWS 12  FEB 22   Status of current WO (PCT) information on STN
 NEWS 13  FEB 22   The IPC thesaurus added to additional patent databases on STN
 NEWS 14  FEB 22   Updates in EPFULL; IPC 8 enhancements added
 NEWS 15  FEB 27   New STN AnaVist pricing effective March 1, 2006
 NEWS 16  FEB 28   MEDLINE/LMEDLINE reload improves functionality
 NEWS 17  FEB 28   TOXCENTER reloaded with enhancements
 NEWS 18  FEB 28   REGISTRY/ZREGISTRY enhanced with more experimental spectral
                   property data
 NEWS 19  MAR 01   INSPEC reloaded and enhanced
 NEWS 20  MAR 03   Updates in PATDPA; addition of IPC 8 data without attributes
 NEWS 21  MAR 08   X.25 communication option no longer available after June 2006
 NEWS 22  MAR 22   EMBASE is now updated on a daily basis

 NEWS EXPRESS  FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,
               CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.
               V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT
               http://download.cas.org/express/v8.0-Discover/

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FILE 'HOME' ENTERED AT 07:23:02 ON 24 MAR 2006

=>
Uploading
THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE
Do you want to switch to the Registry File?
Choice (Y/n):
Switching to the Registry File...
Some commands only work in certain files.  For example, the EXPAND
command can only be used to look at the index in a file which has an
```

index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> FILE REGISTRY

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.63	0.63

FILE 'REGISTRY' ENTERED AT 07:24:55 ON 24 MAR 2006
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STRUCTURE FILE UPDATES: 22 MAR 2006 HIGHEST RN 877759-05-2
DICTIONARY FILE UPDATES: 22 MAR 2006 HIGHEST RN 877759-05-2

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TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

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**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,    *
* effective March 20, 2005.  A new display format, IDERL, is now     *
* available and contains the CA role and document type information.  *
*                                                                    *
**********************************************************************
```

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

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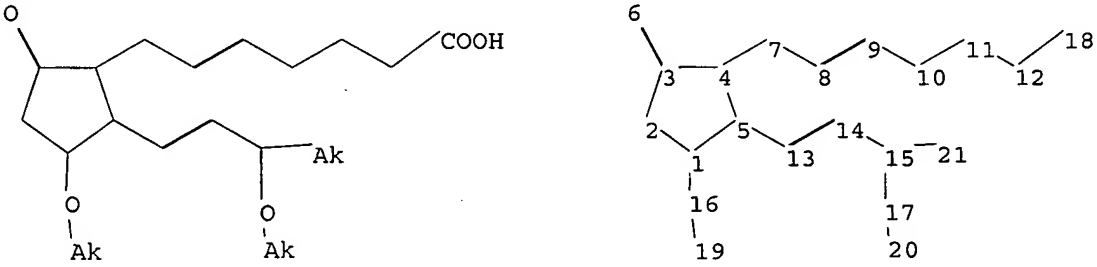
Uploading C:\Documents and Settings\mgraffeo\My Documents\Critical Data\10530752\cmp2.str



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6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
ring nodes :
1 2 3 4 5
chain bonds :

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1-16  3-6  4-7  5-13  7-8  8-9  9-10  10-11  11-12  12-18  13-14  14-15  15-17
15-21  16-19  17-20
ring bonds :
1-2  1-5  2-3  3-4  4-5
exact/norm bonds :
1-2  1-5  1-16  2-3  3-4  3-6  4-5  15-17  15-21  16-19  17-20
exact bonds :
4-7  5-13  7-8  8-9  9-10  10-11  11-12  12-18  13-14  14-15


Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:CLASS  7:CLASS  8:CLASS  9:CLASS
10:CLASS  11:CLASS  12:CLASS  13:CLASS  14:CLASS  15:CLASS  16:CLASS  17:CLASS
18:CLASS  19:CLASS  20:CLASS  21:CLASS



L1      STRUCTURE UPLOADED

=> s l1
SAMPLE SEARCH INITIATED 07:25:05 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      213 TO ITERATE

100.0% PROCESSED      213 ITERATIONS                                2 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          3385 TO     5135
PROJECTED ANSWERS:                2 TO      124

L2            2 SEA SSS SAM L1

=> s l2 full
FULL SEARCH INITIATED 07:25:10 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -     4062 TO ITERATE

100.0% PROCESSED     4062 ITERATIONS                               24 ANSWERS
SEARCH TIME: 00.00.01

L3           24 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                     166.94     167.57

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FILE COVERS 1907 - 24 Mar 2006  VOL 144 ISS 13
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FILE LAST UPDATED: 22 Mar 2006  (20060322/ED)

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=> s l3
L4           42 L3

=> s l4 and (ep3 or prostaglandin or allerg?)
           984 EP3
         68216 PROSTAGLANDIN
         65253 ALLERG?
L5           40 L4 AND (EP3 OR PROSTAGLANDIN OR ALLERG?)

=> s l4 and (ep3 or prostaglandin)
           984 EP3
         68216 PROSTAGLANDIN
L6           40 L4 AND (EP3 OR PROSTAGLANDIN)

=> s l4 (L) ep3
           984 EP3
L7           12 L4 (L) EP3

=> s l4 (L) allerg?
         65253 ALLERG?
L8            1 L4 (L) ALLERG?

=> d

L8   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2006 ACS on STN
AN   2004:333600  CAPLUS
DN   140:344925
TI   Remedies for allergic diseases containing EP3 receptor agonists
IN   Narumiya, Shuh
PA   Ono Pharmaceutical Co., Ltd., Japan
SO   PCT Int. Appl., 60 pp.
     CODEN: PIXXD2
DT   Patent
LA   Japanese
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.         DATE
     --------------      ----   --------    --------------------    --------
PI   WO 2004032964        A1    20040422    WO 2003-JP12980         20031009
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
             GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
             TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     AU 2003272962         A1    20040504    AU 2003-272962          20031009
     EP 1563845            A1    20050817    EP 2003-754059          20031009
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
PRAI JP 2002-297900       A     20021010
     WO 2003-JP12980      W     20031009
OS   MARPAT 140:344925
RE.CNT  14    THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
              ALL CITATIONS AVAILABLE IN THE RE FORMAT
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=> s l7
           984 EP3
L9          12 L4 (L) EP3

=> d 1-12 bib abs hitstr

L9   ANSWER 1 OF 12  CAPLUS  COPYRIGHT 2006 ACS on STN
AN   2005:430242  CAPLUS
DN   142:442242
TI   Prostacyclin attenuates oxidative damage of myocytes by opening
     mitochondrial ATP-sensitive K+ channels via the EP3 receptor
AU   Shinmura, Ken; Tamaki, Kayoko; Sato, Toshiaki; Ishida, Hideyuki; Bolli,
     Roberto
CS   Department of Internal Medicine, Keio University School of Medicine,
     Tokyo, Japan
SO   American Journal of Physiology (2005), 288(5, Pt. 2), H2093-H2101
     CODEN: AJPHAP; ISSN: 0002-9513
PB   American Physiological Society
DT   Journal
LA   English
AB   Prostacyclin (PGI2) and the PGE family alleviate myocardial
     ischemia-reperfusion injury and limit oxidative damage. The
     cardioprotective effects of PGI2 have been traditionally ascribed to
     activation of IP receptors. Recent advances in prostanoid research have
     revealed that PGI2 can bind not only to IP, but also to EP, receptors,
     suggesting cross talk between PGI2 and PGEs. The mechanism(s) whereby
     PGI2 protects myocytes from oxidative damage and the specific receptors
     involved remain unknown. Thus fresh isolated adult rat myocytes were
     exposed to 200 μM H2O2 with or without carbaprostacyclin (cPGI2),
     IP-selective agonists, and ONO-AE-248 (an EP3-selective agonist). Cell
     viability was assessed by trypan blue exclusion after 30 min of H2O2
     superfusion. ONO-AE-248 and cPGI2 significantly improved cell survival
     during H2O2 superfusion; IP-selective agonists did not. The protective
     effect of cPGI2 and ONO-AE-248 was completely abrogated by pretreatment
     with 5-hydroxydecanoate or glibenclamide. In the second series of expts.,
     the mitochondrial ATP-sensitive K+ (KATP) channel opener diazoxide (Dx)
     reversibly oxidized flavoproteins in control myocytes. Exposure to
     prostanoid analogs alone had no effect on flavoprotein fluorescence. A
     second application of Dx in the presence of cPGI2 or ONO-AE-248
     significantly increased flavoprotein fluorescence compared with Dx alone,
     but IP-selective agonists did not. This study demonstrates that PGI2
     analogs protect cardiac myocytes from oxidative stress mainly via
     activation of EP3. The data also indicate that activation of EP3
     receptors primes the opening of mitochondrial KATP channels and that this
     mechanism is essential for EP3-dependent protection.
IT   211230-67-0, ONO-AE-248
     RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); BIOL
     (Biological study)
        (prostacyclin attenuation of oxidative damage of rat cardiomyocytes by
        opening mitochondrial ATP-sensitive potassium channels via EP3
        receptors)
RN   211230-67-0  CAPLUS
CN   Prosta-5,13-dien-1-oic acid, 11,15-dimethoxy-9-oxo-,
     (5Z,11α,13E,15S)- (9CI)  (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.
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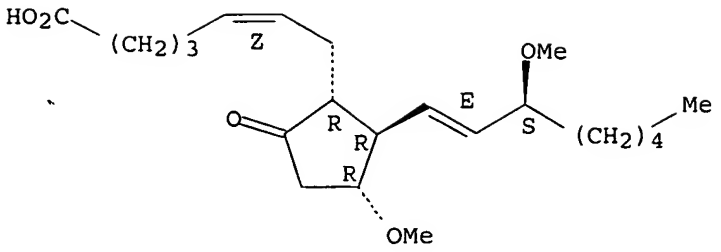


RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:96459 CAPLUS
DN 142:148832
TI Remedy for cartilage-related diseases containing EP2 and/or EP3 agonist
IN Toguchida, Junya
PA Ono Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 122 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2005009468	A1	20050203	WO 2004-JP10890	20040723

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI JP 2003-280191 A 20030725

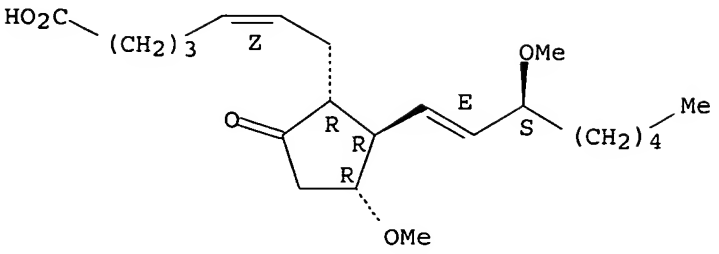
AB Disclosed is a remedy for cartilage-related diseases containing as the active ingredient a substance having an agonistic activity to prostaglandin receptor EP2 and/or EP3. A substance having an agonistic activity to EP2 and/or EP3 has effects of promoting chondrogenesis, promoting chondrocyte growth, promoting chondrocyte differentiation, inhibiting cartilage calcification and inhibiting cartilage degradation, or effects of promoting integrin mRNA expression, promoting fibronectin mRNA expression, promoting cyclin D1 mRNA expression and inhibiting osteopontin mRNA expression, and, therefore, is useful as a remedy for cartilage-related diseases. The remedy of the present invention is also usable in production of cartilage implant. The effect of an EP2 agonist (5Z,9β,11α,13E)-17,17-Propano-11,16-dihydroxy-9-chloro-20-norprosta-5,13-dienoic acid (I) on human chondrocyte proliferation was in vitro tested. Also a tablet containing I 0.5 mg/tablet was formulated.

IT **211230-67-0**, ONO-AE-248
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(remedy for cartilage-related diseases containing EP2 and/or EP3 agonist)

RN 211230-67-0 CAPLUS
CN Prosta-5,13-dien-1-oic acid, 11,15-dimethoxy-9-oxo-, (5Z,11α,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



RE.CNT 81 THERE ARE 81 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:872709 CAPLUS
DN 141:343520
TI Remedy for spinal canal stenosis
IN Takenobu, Yoshifumi; Kamanaka, Yoshihisa; Obata, Takaaki
PA Ono Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004089411	A1	20041021	WO 2004-JP4836	20040402
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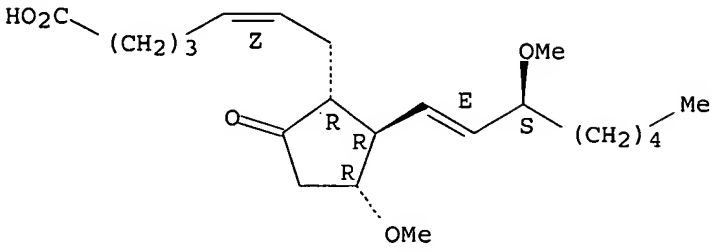
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1609480	A1	20051228	EP 2004-725524	20040402
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
PRAI	JP 2003-100388	A	20030403		
	WO 2004-JP4836	W	20040402		

OS MARPAT 141:343520
AB Disclosed is a remedy for spinal canal stenosis which comprises a combination of a compound having EP2 agonism with a compound having EP3 agonism. A drug comprising a combination of a compound having EP2 agonism with a compound having EP3 agonism shows an efficacy in a rat gait disorder model induced by compression of cauda equina. Namely, it is efficacious against spinal canal stenosis to use a combination of a compound having EP2 agonism with a compound having EP3 agonism or a compound having both of EP2 agonism and EP3 agonism. Animal studies and formulations were provided using (5Z,9β,11α,13E)-17,17-propano-11,16-dihydroxy-9-chloro-20-norprosta-1,13-diene lysine salt and 11α,15α-Dimethoxy-9-oxoprosta-5Z,13E-dienoic acid.
IT **211230-67-0**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(spinal canal stenosis treatment with EP2 and **EP3** agonists in combination with addnl. active agents)
RN 211230-67-0 CAPLUS
CN Prosta-5,13-dien-1-oic acid, 11,15-dimethoxy-9-oxo-,

(5Z,11α,13E,15S)- (9CI) (CA INDEX NAME)

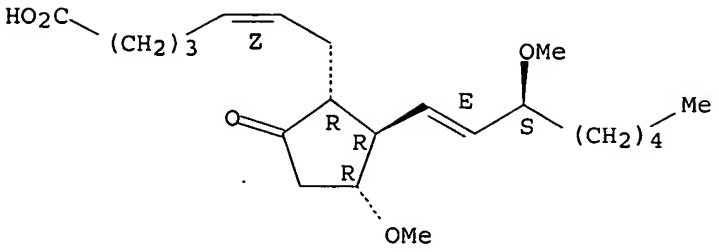
Absolute stereochemistry.
Double bond geometry as shown.



RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:866782 CAPLUS
DN 141:389181
TI Vasoconstriction induced by activation of EP1 and EP3 receptors in human lung: effects of ONO-AE-248, ONO-DI-004, ONO-8711 or ONO-8713
AU Norel, Xavier; de Montpreville, Vincent; Brink, Charles
CS Hopital Broussais, CNRS UMR7131, Paris, 75014, Fr.
SO Prostaglandins & Other Lipid Mediators (2004), 74(1-4), 101-112
CODEN: POLMFL; ISSN: 1098-8823
PB Elsevier B.V.
DT Journal
LA English
AB This study investigated the effects and selectivity of ONO-AE-248, ONO-DI-004, ONO-8711 and ONO-8713 on EP1 and EP3 receptors in human pulmonary vessels. The prostanoid receptors involved in the vasoconstriction of human pulmonary arteries (HPA) are TP and EP3 whereas in pulmonary veins (HPV), this response is associated with TP and EP1. The expts. were performed in presence of BAY u3405 (TP antagonist). ONO-DI-004 (EP1 agonist) and ONO-AE-248 (EP3 agonist), exhibited little or no activity in HPV, whereas contractions were induced in HPA with ONO-AE-248. In HPV, the contractions produced with sulprostone (EP1,3 agonist) were blocked in a non competitive manner by both EP1 antagonists (ONO-8711, 30 μM; ONO-8713, 10 μM). The involvement of EP1 mediated contraction in HPV was also observed during the vasorelaxations induced with PGE1 and 5-cis-carba-PGI2. In pre-contracted HPV treated with AH6809 (30 μM; EP1 antagonist) the PGE1 vasorelaxations were potentiated, while unchanged in HPA. These results demonstrate the selectivity of ONO-AE-248 for the EP3 receptor in HPA, ONO-DI-004 was ineffective on the EP1 receptor present in HPV while ONO-8713 was the more potent EP1 antagonist used in this tissue.
IT **211230-67-0**, ONO-AE-248
RL: BUU (Biological use, unclassified); PAC (Pharmacological activity); BIOL (Biological study); USES (Uses)
(ONO-AE-248, ONO-DI-004, ONO-8711 and ONO-8713 effects and selectivity on EP1 and **EP3** receptors in human pulmonary vessel vasoconstriction)
RN 211230-67-0 CAPLUS
CN Prosta-5,13-dien-1-oic acid, 11,15-dimethoxy-9-oxo-, (5Z,11α,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RE.CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

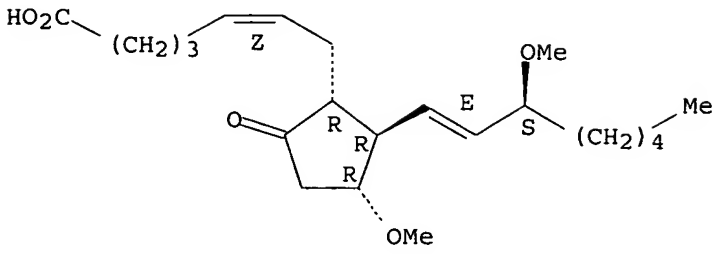
L9 ANSWER 5 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:333600 CAPLUS
DN 140:344925
TI Remedies for allergic diseases containing EP3 receptor agonists
IN Narumiya, Shuh
PA Ono Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004032964	A1	20040422	WO 2003-JP12980	20031009
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2003272962	A1	20040504	AU 2003-272962	20031009
	EP 1563845	A1	20050817	EP 2003-754059	20031009
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRAI	JP 2002-297900	A	20021010		
	WO 2003-JP12980	W	20031009		

OS MARPAT 140:344925
AB Disclosed is a preventive and/or a remedy for allergic diseases containing a compound having an agonistic activity to EP3 receptor which is one of prostaglandin E2 receptor subtypes. More specifically speaking, a compound having an agonistic activity to EP3 receptor is efficacious in treating allergic respiratory diseases such as bronchial asthma, infantile asthma, allergic asthma and atopic asthma. Moreover, it is expected that a highly selective compound would exert a more remarkable therapeutic effect. The effect of 11α,15α-dimethoxy-9-oxoprosta-5Z,13E-dienoic acid (I) in OVA-induced asthma model mice was examined Also, a tablet containing I 0.5 mg/tablet was prepared
IT **211230-67-0**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(remedies for allergic diseases containing **EP3** receptor agonists)
RN 211230-67-0 CAPLUS
CN Prosta-5,13-dien-1-oic acid, 11,15-dimethoxy-9-oxo-, (5Z,11α,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

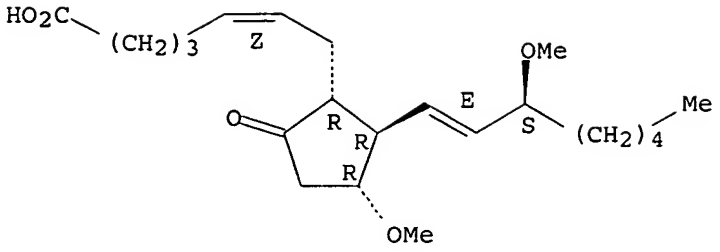
Double bond geometry as shown.



RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:426197 CAPLUS
DN 139:208133
TI Effects of 8-iso-prostaglandin E2 and 8-iso-prostaglandin F2α on the release of noradrenaline from the isolated rat stomach
AU Nakamura, Kumiko; Okada, Shoshiro; Ono, Kaori; Yokotani, Kunihiko
CS Department of Pharmacology, Kochi Medical School, Nankoku, Kochi, 783-8505, Japan
SO European Journal of Pharmacology (2003), 470(1-2), 73-78
CODEN: EJPHAZ; ISSN: 0014-2999
PB Elsevier Science B.V.
DT Journal
LA English
AB In the present experiment, the authors examined the effect of 8-iso-prostaglandin E2 and 8-iso-prostaglandin F2α on the release of noradrenaline from the isolated rat stomach. The postganglionic sympathetic nerves were elec. stimulated twice at 1 Hz for 1 min and test reagents were added during the second stimulation. Addition of 8-iso-prostaglandin E2 (10-8-10-6 M) and 8-iso-prostaglandin F2α (10-7-10-5 M) dose-dependently reduced the evoked noradrenaline release, and these inhibitory potencies were as follows: 8-iso-prostaglandin E2 > 8-iso-prostaglandin F2α. The inhibitory effect of 8-iso-prostaglandin F2α, but not 8-iso-prostaglandin E2, was abolished by 10-6 M SQ-29548 ([1S-[1α,2α(Z),3α,4α]]-7-[3-[[2-[(phenylamino)carbonyl]hydrazino] methyl]-7-oxabicyclo[2,2,1]hept-2-yl]-5-heptenoic acid) (a prostanoid TP receptor antagonist). The inhibitory effect of 8-iso-prostaglandin E2 was abolished by 10-5 M AH-6809 (6-isopropoxy-9-oxoxanthene-2-carboxylic acid) (a prostanoid EP receptor antagonist), which also attenuated the inhibitory effects of ONO-AE-248 (16S-9-deoxy-9β-chloro-15-deoxy-16-hydroxy-17,17-trimethylene 19, 20-didehydro prostaglandin F2) (a selective EP3 receptor agonist) on the evoked release of noradrenaline. The inhibitory effect of 8-iso-prostaglandin F2α, but not 8-iso-prostaglandin E2, was abolished by pertussis toxin. These results suggest that 8-iso-prostaglandin F2α inhibits noradrenaline release through TP receptors, whereas 8-iso-prostaglandin E2 seems to inhibit noradrenaline release through EP3 receptors, located on the gastric sympathetic nerve terminals in rats.
IT **211230-67-0**, ONO-AE-248
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(EP3 receptor agonist; iso-PGE2 and iso-PGF2α effect on noradrenaline release from isolated rat stomach and mechanisms thereof)
RN 211230-67-0 CAPLUS
CN Prosta-5,13-dien-1-oic acid, 11,15-dimethoxy-9-oxo-, (5Z,11α,13E,15S)- (9CI) (CA INDEX NAME)

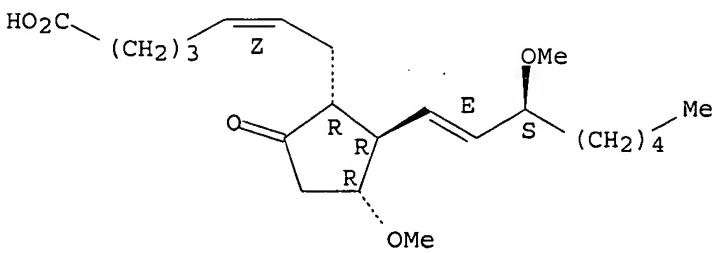
Absolute stereochemistry.
Double bond geometry as shown.



RE.CNT 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:231920 CAPLUS
DN 139:63721
TI Contrasting effects of E type prostaglandin (EP) receptor agonists on core body temperature in rats
AU Oka, Takakazu; Oka, Kae; Saper, Clifford B.
CS Department of Neurology and Program in Neuroscience, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, 02115, USA
SO Brain Research (2003), 968(2), 256-262
CODEN: BRREAP; ISSN: 0006-8993
PB Elsevier Science B.V.
DT Journal
LA English
AB Prostaglandin E2 (PGE2) is thought to be a principal fever mediator. There are four subtypes of PGE (EP) receptors, EP1-EP4. The authors investigated which EP receptors mediate PGE2-induced hyperthermia by injecting selective EP receptor agonists into the rat lateral cerebral ventricle under unrestrained condition. ONO-DI-004, an EP1 receptor agonist, increased the core temperature (Tc) in a dose-dependent manner (1.6° at 20 nmol, with the peak 30 min after injection) with a time course similar to PGE2-induced hyperthermia. ONO-AE1-259-01 (20 nmol), an EP2 receptor agonist, did not change the Tc. ONO-AE-248 (20 nmol), an EP3 receptor agonist, also increased the Tc. However, the peak effect was delayed (1.2°, 50 min after injection) compared to PGE2. In contrast, ONO-AE1-329, an EP4 receptor agonist, decreased the Tc. These findings suggest that the EP1, EP3, and EP4 receptors all may contribute to the thermoregulatory response to PGE2, but each may have a different role.
IT **211230-67-0**, ONO-AE-248
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(EP3 receptor agonist; contrasting effects of E type prostaglandin EP receptor agonists central administration on core body temperature in rats)
RN 211230-67-0 CAPLUS
CN Prosta-5,13-dien-1-oic acid, 11,15-dimethoxy-9-oxo-, (5Z,11α,13E,15S)- (9CI) (CA INDEX NAME)

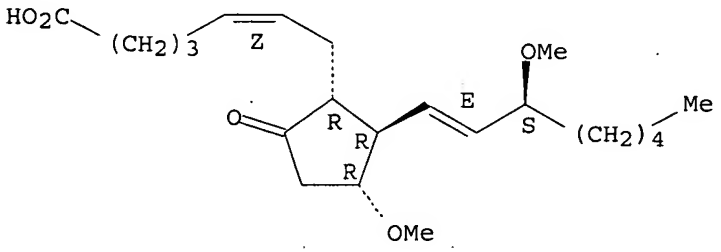
Absolute stereochemistry.
Double bond geometry as shown.



RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:8043 CAPLUS
DN 138:332106
TI Prostanoid EP3 and TP receptors-mediated inhibition of noradrenaline release from the isolated rat stomach
AU Yokotani, Kunihiko; Nakamura, Kumiko; Okada, Shoshiro
CS Department of Pharmacology, Kochi Medical School, Nankoku, Kochi, 783-8505, Japan
SO European Journal of Pharmacology (2003), 459(2-3), 187-193
CODEN: EJPHAZ; ISSN: 0014-2999
PB Elsevier Science B.V.
DT Journal
LA English
AB The postganglionic sympathetic nerves of the isolated rat stomach were elec. stimulated twice at 1 Hz for 1 min. Prostaglandin E2 and ONO-AE-248 (16S-9-deoxy-9β-chloro-15-deoxy-16-hyfroxy-17,17-trimethylene-19,20-didehydro prostaglandin F2) (an EP3 receptor agonist) reduced the evoked noradrenaline release, while ONO-DI-004 (17S-2,5-ethano-6-oxo-17,20-dimethyl prostaglandin E1) (an EP1 receptor agonist), ONO-AE1-259-01 (11,15-O-dimethyl prostaglandin E2) (an EP2 receptor agonist) and ONO-AE1-329 [16-(3-methoxymethyl)phenyl-ω-tetranor-3,7-dithia prostaglandin E1] (an EP4 receptor agonist) had no effect. U-46619 (9,11-dideoxy-9α,11α-methanoepoxy prostaglandin F2α) and I-BOP (7-[3-[3-hydroxy-4-(4-iodophenoxy)-1-butenyl]-7-oxabicyclo[2,2,1]hept-2-yl]-,[1S[1α,2α(Z),3β(1E,3S)4α]]-5-heptenoic acid) (TP receptor agonists) also reduced the noradrenaline release and these inhibitory effects were abolished by SQ-29548 (a TP receptor antagonist). The inhibitory effect of U-46619, but not ONO-AE-248, was abolished by pertussis toxin. These results suggest that the prostanoid EP3 and TP receptors mediate the inhibition of gastric noradrenaline release; TP, but not EP3, receptor-mediated inhibition is mediated by a pertussis toxin-sensitive mechanism in rats.
IT **211230-67-0**, ONO-AE-248
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prostanoid **EP3** and TP receptors-mediated inhibition of noradrenaline release from gastric sympathetic nerve terminal in isolated rat stomach)
RN 211230-67-0 CAPLUS
CN Prosta-5,13-dien-1-oic acid, 11,15-dimethoxy-9-oxo-, (5Z,11α,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:380457 CAPLUS
DN 137:164047

TI In vitro pharmacological characterization of the prostanoid receptor population in the non-pregnant porcine myometrium

AU Cao, Jinshan; Shayibuzhati, Mikeremu; Tajima, Tsuyoshi; Kitazawa, Takio; Taneike, Tetsuro

CS School of Veterinary Medicine, Department of Pharmacology, Rakuno Gakuen University, Ebetsu, Hokkaido, 069-8501, Japan

SO European Journal of Pharmacology (2002), 442(1-2), 115-123
CODEN: EJPHAZ; ISSN: 0014-2999

PB Elsevier Science B.V.

DT Journal

LA English

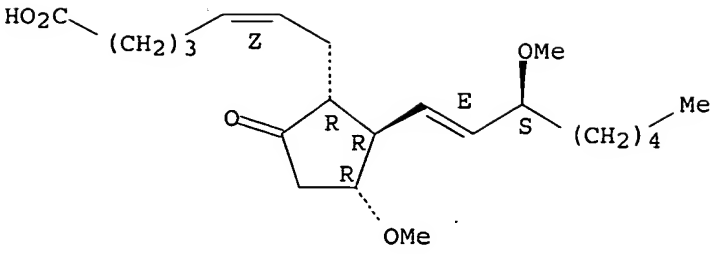
AB To characterize prostanoid receptors present in the non-pregnant porcine uterus, the effects of naturally occurring prostaglandins (D2, E2, F2α, I2) and synthetic prostanoid receptor agonists on contractility of the longitudinal and circular muscles were examined in vitro. The potent contractile actions of prostaglandin F2α and cloprostenol indicate the presence of excitatory FP receptors in the porcine uterus. The longitudinal muscle was more sensitive to FP receptor agonists than was the circular muscle. Prostaglandin D2 produced an excitatory response in the longitudinal muscle but completely inhibited the spontaneous contraction of the circular muscle. BW-245C (5-(6-carboxyhexyl)-1-(3-cyclohexyl-3-hydroxypropyl)hydantoin, 1 nM-10 μM, a DP receptor agonist) inhibited the spontaneous contractions of both muscles, but the inhibition was conspicuously stronger in the circular muscle. Prostaglandin I2 caused excitatory and inhibitory responses in the longitudinal and circular muscles, resp., at relatively high concns. (10-100 μM). Cicaprost, an IP receptor agonist caused inhibition of the contraction in the circular muscle but contracted the longitudinal muscle. Iloprost, an EP1/IP receptor agonist, caused excitatory responses in both muscles at relative high concns. Prostaglandin E2 caused excitatory responses at 1-100 nM and inhibitory responses at 100 nM-10 μM in both muscle layers. ONO-DI-004 ((17S)-2,5-ethano-6-oxo-17,20-dimethyl prostaglandin E1, an EP1 receptor agonist) and ONO-AE-248 ((16S)-9-deoxy-9β-chloro-15-deoxy-16-hydroxy-17,17-trimethylene-19,20-didehydro prostaglandin F2, an EP3 receptor agonist) contracted the longitudinal muscle but had little effect on the circular muscle. ONO-AE1-259 (11,15-O-dimethyl prostaglandin E2, an EP2 receptor agonist) inhibited the spontaneous contractions of both muscle layers to almost the same degree, but ONO-AE1-329 (16-(3-methoxymethyl)phenyl-ω-tetranor-3,7-dithia prostaglandin E1, an EP4 receptor agonist) did not inhibit the myometrial contraction. The present results indicate that contractile (FP, EP1, EP3) and relaxatory (DP, IP, EP2) prostanoid receptors are present in the non-pregnant porcine uterus. There are marked muscle layer-related differences in the degree of responsiveness of prostanoid receptor agonists, and these differences suggest that there is a heterogeneous distribution of prostanoid receptors in the longitudinal and circular muscles (FP, EP1 and EP3, longitudinal muscle > circular muscle; DP, circular muscle > longitudinal muscle).

IT **211230-67-0**, ONO-AE-248
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**EP3** receptor agonist; in vitro pharmacol. characterization of prostanoid receptor population in non-pregnant porcine myometrium circular and longitudinal muscle)

RN 211230-67-0 CAPLUS

CN Prosta-5,13-dien-1-oic acid, 11,15-dimethoxy-9-oxo-, (5Z,11α,13E,15S)- (9CI) (CA INDEX NAME)

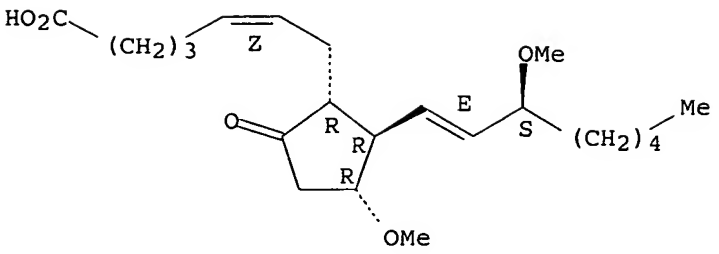
Absolute stereochemistry.
Double bond geometry as shown.



RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 10 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:95245 CAPLUS
DN 136:273510
TI Involvement of postsynaptic EP4 and presynaptic EP3 receptors in actions of prostaglandin E2 in rat supraoptic neurones
AU Shibuya, I.; Setiadji, S. V.; Ibrahim, N.; Harayama, N.; Maruyama, T.; Ueta, Y.; Yamashita, H.
CS Department of Physiology, University of Occupational and Environmental Health, Kitakyushu, Japan
SO Journal of Neuroendocrinology (2002), 14(1), 64-72
CODEN: JOUNE2; ISSN: 0953-8194
PB Blackwell Publishing Ltd.
DT Journal
LA English
AB We have reported that supraoptic nucleus (SON) neurons are excited by prostaglandin E2 (PGE2) presumably via dual postsynaptic PG receptors, FP receptors and unidentified EP receptors, and that presynaptic EP receptors may also be involved in the excitation. In the present study, to clarify the receptor mechanism of the PGE2-mediated actions on SON neurons, we studied the pre- and postsynaptic effects of four newly developed EP agonists that are selective for each of the four EP receptors, EP1-4, on rat SON neurons using extracellular recording and whole-cell patch-clamp techniques. The EP4 agonist ONO-AE1-329 mimicked the excitatory effects of PGE2, whereas the EP1 agonist ONO-DI-004, the EP2 agonist ONO-AE1-257 and the EP3 agonist ONO-AE-248 had little or no effect. The effects of ONO-AE1-329 were unaffected by the EP1/FP/TP antagonist, ONO-NT-012, which potently suppressed the excitation caused by the FP agonist fluprostenol and PGE2. ONO-AE1-329 caused marked excitation when responses to fluprostenol were desensitized by repeated applications of fluprostenol. Patch-clamp anal. in SON neurons showed that ONO-AE1-329 induced inward currents at a holding potential of -70 mV and the reversal potential of the currents was -35.1 mV. On the other hand, the frequency of spontaneous inhibitory postsynaptic currents recorded from SON slice prepns. was suppressed by ONO-AE-248, but unaffected by the other three EP agonists. These results suggest that SON neurons possess postsynaptic EP4 receptors and that γ-aminobutyric acid neurons innervating SON neurons possess presynaptic EP3 receptors in their terminals. Activation of the two EP receptors may be involved in the excitatory regulation of SON neurons by PGE2.
IT **211230-67-0**, ONO-AE-248
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(postsynaptic EP4 and presynaptic **EP3** receptors in actions of prostaglandin E2 in rat supraoptic neurons)
RN 211230-67-0 CAPLUS
CN Prosta-5,13-dien-1-oic acid, 11,15-dimethoxy-9-oxo-, (5Z,11α,13E,15S)- (9CI) (CA INDEX NAME)

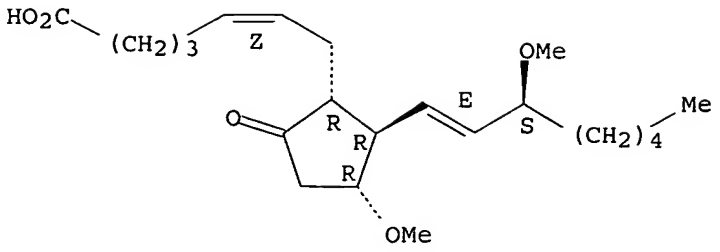
Absolute stereochemistry.
Double bond geometry as shown.



RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:430099 CAPLUS
DN 135:175924
TI Characterization of EP receptor subtypes responsible for prostaglandin E2-induced pain responses by use of EP1 and EP3 receptor knockout mice
AU Minami, Toshiaki; Nakano, Hiroyuki; Kobayashi, Takuya; Sugimoto, Yukihiko; Ushikubi, Fumitaka; Ichikawa, Atsushi; Narumiya, Shuh; Ito, Seiji
CS Department of Anesthesiology, Osaka Medical College, Takatsuki, 569-8686, Japan
SO British Journal of Pharmacology (2001), 133(3), 438-444
CODEN: BJPCBM; ISSN: 0007-1188
PB Nature Publishing Group
DT Journal
LA English
AB Prostaglandin E2 (PGE2) is known to be the principal pro-inflammatory prostanoid and play an important role in nociception. To identify PGE receptor (EP) subtypes that mediate pain responses to noxious and innocuous stimuli, the authors studied them by use of EP1 and EP3 knockout (EP1-/- and EP3-/-) mice. PGE2 could induce mech. allodynia in EP1+/+, EP3+/+ and EP3-/- mice, but not in EP1-/- mice. N-methyl-D-aspartate (NMDA), the substrate of nitric oxide (NO) synthase L-arginine, or the NO donor sodium nitroprusside administered intrathecal (i.t.) could induce allodynia in EP3-/- and EP1-/- mice. Activation of EP1 receptors appears to be upstream, rather than downstream, of NMDA receptor activation and NO production in the PGE2-induced allodynia. Although PGE2 produced thermal hyperalgesia over a wide range of dosages from 50 pg to 0.5 μg kg-1 in EP3+/+ mice, it showed a monophasic hyperalgesic action at 5 ng kg-1 or higher doses in EP3-/- mice. The selective EP3 agonist, ONO-AE-248, induced hyperalgesia at 500 pg kg-1 in EP3+/+ mice, but not in EP3-/- mice. Saline-injected EP1-/- mice showed hyperalgesia, which was reversed by i.t. PGE2 in a dose-dependent manner. There was no significant difference in the formalin-induced behaviors between EP1-/- or EP3-/- mice and the cognate wild-type mice. These results demonstrate that spinal EP1 receptors are involved in the PGE2-induced allodynia and that spinal EP3 receptors are involved in the hyperalgesia induced by low doses of PGE2. However, the formalin-induced pain cannot be ascribed to a single EP receptor subtype EP1 or EP3.
IT **211230-67-0**, ONO-AE-248
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(characterization of prostanoid EP receptor subtypes responsible for prostaglandin E2 induced pain responses by use of EP1 and **EP3** receptor knockout mice)
RN 211230-67-0 CAPLUS
CN Prosta-5,13-dien-1-oic acid, 11,15-dimethoxy-9-oxo-, (5Z,11α,13E,15S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 12 OF 12 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1999:617854 CAPLUS
DN 132:19149
TI Selective activation of the prostanoid EP3 receptor reduces myocardial infarct size in rodents
AU Zacharowski, Kai; Olbrich, Antje; Piper, Julie; Hafner, Gerd; Kondo, Kigen; Thiemermann, Christoph
CS William Harvey Research Institute, St Bartholomew's and the Royal London School of Medicine and Dentistry, London, EC1 M 6BQ, UK
SO Arteriosclerosis, Thrombosis, and Vascular Biology (1999), 19(9), 2141-2147
CODEN: ATVBFA; ISSN: 1079-5642
PB Lippincott Williams & Wilkins
DT Journal
LA English
AB The cardioprotective effects of E-type prostaglandins (EPs) have been attributed to vasodilatation, inhibition of platelet and neutrophil function (EP2 mediated), and an unknown cytoprotective effect. The authors have hypothesized that selective activation of EP3 receptors may cause cardioprotection. The prostanoid derivative ONO-AE-248 selectively binds to murine EP3α receptors expressed in Chinese hamster ovary (CHO) cells (Ki, 15 nmol/L) and prevents the rise in cAMP caused by forskolin in CHO cells (IC50 ≈1 nmol/L) in which the EP3α receptor had been expressed. In anesthetized rats subjected to regional myocardial ischemia for 25 or 45 min and 2 h of reperfusion, infusion of ONO-AE-248 (5 μg/kg/min, i.v.) caused a significant reduction in infarct size from 60% to 36% and from 78% to 58%, resp. The reduction in infarct size caused by ONO-AE-248 in rats subjected to 25 min of ischemia and reperfusion was abolished by a selective inhibitor of ATP-sensitive K (KATP) channels, 5-hydroxydecanoate, and the protein kinase C inhibitors staurosporine and chelerythrine. In anesthetized rabbits subjected to coronary artery occlusion for 45 or 60 min and 2 h of reperfusion, infusion of ONO-AE-248 (5 μg/kg/min, i.v.) caused a significant reduction in infarct size from 61% to 36% and from 63% to 42%, resp. The reduction in infarct size caused by ONO-AE-248 in the rabbit was also abolished by 5-hydroxydecanoate. The cardioprotective effect of ONO-AE-248 in rats or rabbits was not associated with any hemodynamic effects. Selective activation of the prostanoid EP3 receptor reduces myocardial infarct size in rodents by a mechanism(s) that may involve the activation of protein kinase C and the opening of KATP channels.
IT **211230-67-0**, ONO-AE 248
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**EP3** receptor activation reduces myocardial infarct size in rodents)
RN 211230-67-0 CAPLUS
CN Prosta-5,13-dien-1-oic acid, 11,15-dimethoxy-9-oxo-, (5Z,11α,13E,15S)- (9CI) (CA INDEX NAME)

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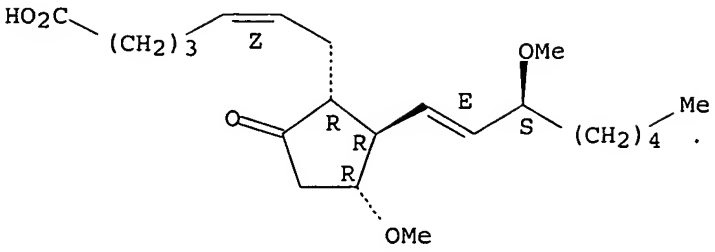

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30341 ASTHMA
L10 1 L7 AND ASTHMA

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NEWS 4 DEC 23 New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/